Experimental Microbeam Radiation Therapy Passes Latest Test, Draws Nearer Ultimate Goal: Treating Brain Tumors in Children

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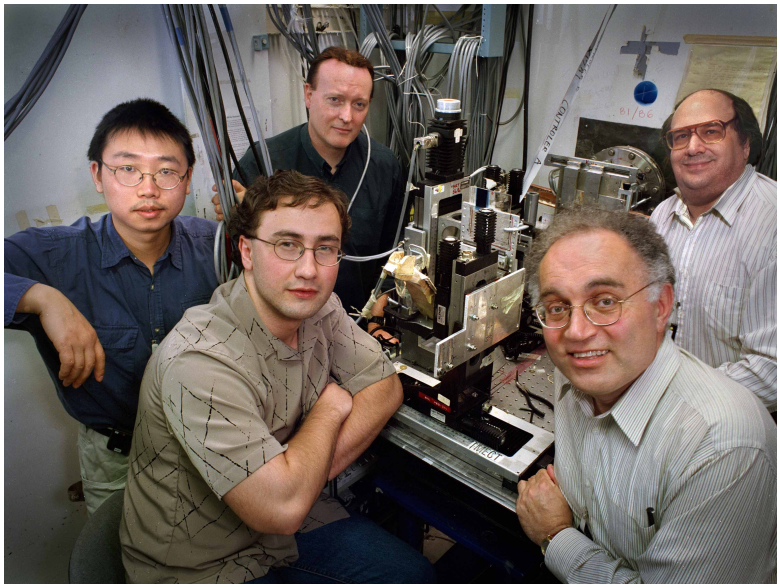
An experimental form of radiation therapy, known as microbeam radiation therapy (MRT) and now under development at Brookhaven Lab, appears to be less damaging to healthy brain tissue than traditional radiation therapy.

In a study appearing in a recent issue of *Cellular and Molecular Biology*, BNL scientists present evidence that the brains of embryonic ducks, studied as a model for human infants, have a remarkably higher tolerance to microbeam radiation than to conventional radiation beams.

The therapy has not yet been tested in humans and is probably years away from clinical application. But Avraham Dilmanian of the Medical Department, who is leading the studies, says, "The hope is that, eventually, we will be able to use microbeam arrays to destroy pediatric brain tumors, or at least significantly delay their growth, without damaging as much surrounding tissue as conventional, broad-beam x-rays do."

Other BNL collaborators who are or have worked with Dilmanian on this project included: Gerard Morris, Géraldine Le Duc, Xiaoling Huang, Baori Ren, Tigran Bacarian, Itzhak Orion, Pravin Sathé, and Xiao-Ye Wu of the Medical Department, and Zhong Zhong of the National Synchrotron Light Source (NSLS). The scientists are looking for a treatment for brain tumors in infants and young children. Because developing brains are particularly susceptible to radiation damage, conventional radiation therapy cannot be used on children before the age of three and is used judiciously afterward.



Seated around the experimental microbeam radiation therpy (MRT) bench at the NSLS X17B1 beamline are the current MRT team: (from left) Nan Zhong and Renat Yakupov, both of the Medical Department; Gerald Morris, University of Oxford and BNL; Avraham Dilmanian, Medical; and Eliot Rosen, Long Island Jewish (LIJ) Medial Center. Not in the picture are: Louis Peña and Tigran Bacarian, Medical; and Alexander Fuchs, LIJ.

In MRT, x-rays are confined to very thin slices of planar beams arranged in parallel arrays with spaces in between, as are the parallel panels of open vertical blinds. As a result, the x-rays irradiate only about one third of the tissue, and the areas between the beam slices receive very little radiation.

The technique was first developed at the NSLS in the early 1990s. It is still under investigation there and at the European Synchrotron Radiation Facility in Grenoble, France. Unlike x-ray sources used in clinical radiation therapy, only high-intensity synchrotron sources can be used to confine the beam to the extremely narrow slices with very high dose rates that are needed for MRT.

In the study, the duck embryos treated with microbeam radiation fared much better than those treated with broad-beam radiation. “The ducks’ brains were about ten times more tolerant to the microbeam radiation than the broad beams,” Dilmanian says.

“Even when the un-irradiated areas between the microbeam slices are taken into account, that is, when the dose is averaged over the entire area treated, microbeams still have an approximately three-fold advantage over broad-beams in terms of normal brain tissue tolerance,” he says.

Previous experiments by Daniel Slatkin, retired from Medical; Jean Laissue, University of Bern, Switzerland; the late Per Spanne, formerly of the Department of Applied Science; and Dilmanian and others have shown that these same microbeam doses can destroy or slow the growth of highly malignant brain tumors in rats, at doses that cause very little damage to the surrounding normal brain tissue. Furthermore, in those studies, the treatment was accomplished by irradiating the tumors from only one direction and in one treatment. This is in contrast to conventional radiation treatment, which is carried out from different angles and over as many as 40 sessions.

The scientists hypothesize that, in MRT, some of the endothelial cells—cells that line blood capillaries—survive in the interbeam regions. In normal tissue, these cells appear to replace the neighboring cells killed by the beam. But, in tumors, this recovery process may be impaired, so the blood flow stops, and the tumor is starved to death.

The next step will be to investigate the biological mechanisms by which unidirectional MRT preferentially damages brain tumor tissue while it spares the normal brain tissue. Understanding these mechanisms is essential if MRT is to proceed toward clinical use.

This research was funded by DOE and the Children’s Brain Tumor Foundation. Current collaborators include: Gerard Morris, Nan Zhong, Louis Peña, Tigran Bacarian, and Renat Yakupov of Medical, and Eliot Rosen and Alexander Fuchs of Long Island Jewish Medical Center in New Hyde Park, New York.

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